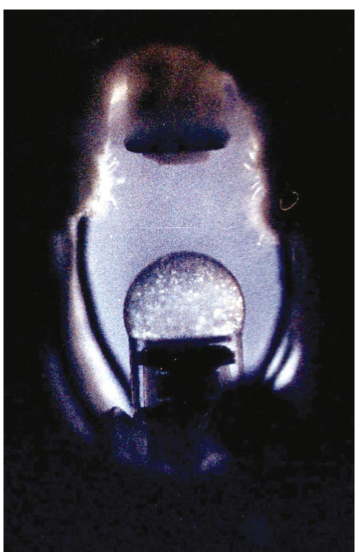
Getting to the Heart of the Matter

Protein Crystal Growth

The basic mechanics of living organisms, such as humans, are fairly well understood by doctors and scientists. Circulation systems send nutrients and other needed materials throughout the organism, muscles help provide movement through stretching and contracting, and digestive systems convert raw material into needed components that keep the system running.

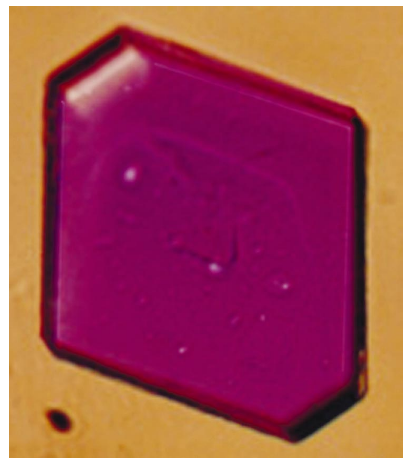
Yet, within each organism is a hidden world of proteins that make all of this possible. Proteins are the building blocks of all life, and how they react with one another in living organisms determines many things, including if a creature will be healthy or get sick. Understanding this hidden world of proteins and their interactions is, needless to say, of intense interest to scientists and doctors.



Using the process known as vapor diffusion, scientists can grow crystals to be used for X-ray diffraction experiments to determine the atomic structure of crystals.

Proteins are complex compounds that are made up of one or more chains of amino acids. Amino acids are simpler compounds that contain carbon, oxygen, nitrogen, and hydrogen atoms. Compounds are the union of two or more elements into a substance that can not be physically separated.

Within the human body, there are thousands of different proteins. Proteins serve a variety of functions in all living organisms. Proteins make it possible for red blood cells to carry oxygen throughout the body, and help transmit nerve impulses so we can hear, smell, taste, and feel the world around us. On the other hand, diseases involve proteins, either directly or indirectly. These can be in the form of hormonal irregularities, toxins produced by invading organisms, or proteins an invading organism needs to survive, prosper, and replicate.



A crystal of Factor D, the protein in the human body that helps activate the immune system when foreign objects are detected.

Each protein has a particular chemical structure, which means that it has a unique "shape." This shape is not smooth, but is rough, with chemical "arms" or structures sticking out. It is these structures that allow each protein to do its job by interacting with chemicals or binding with other proteins. If researchers can determine the shape, or shapes, of a protein, they can learn how it works. Once this is understood, researchers can then find ways to help or hinder a given protein.

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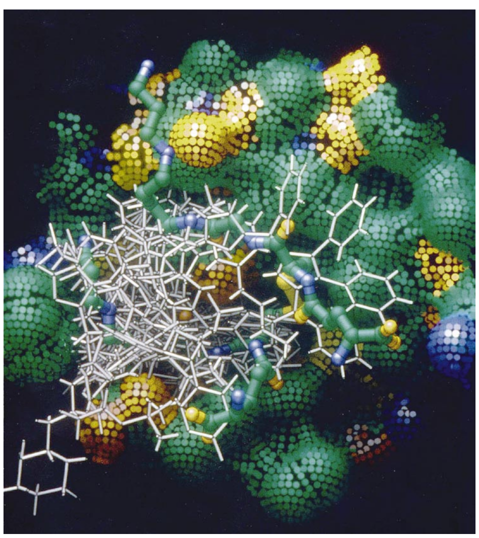
Background Information

Science

While there are several ways in which researchers can determine the structure of a protein, the most widely used method is protein crystallography. Proteins can be made to crystallize in much the same way sugar crystals can be formed from sugar water to make rock candy.

If you were to mix sugar into warm water, then place a string or wooden stick into the mixture and let it sit undisturbed, you would see crystals begin to grow. These crystals form because the concentration of the sugar increases as the water evaporates, and when the concentration of sugar is more than the remaining water can hold, the sugar crystallizes onto the string or stick. The resulting crystals will continue to grow in size as the process continues, making the sweet treat known as rock candy.

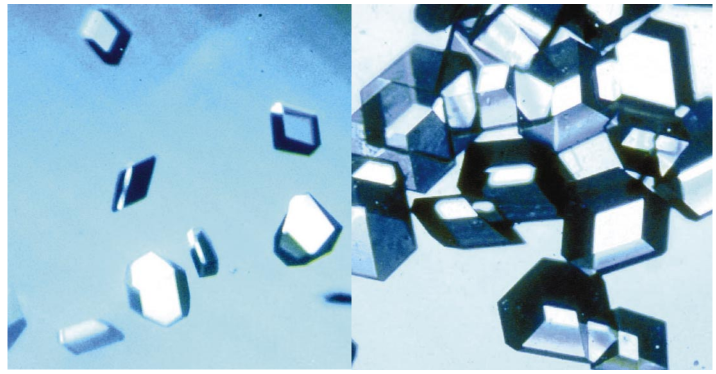
Just as water evaporates from the sugar solution and forms sugar crystals, protein crystallographers use a similar process to form protein crystals. This process is called vapor diffusion. A protein to be crystallized is in a solution that contains water. As water migrates from the drop in the protein crystal growth chamber to the air and wicking material, the protein solution becomes concentrated and protein crystals begin to form. As the experiment continues, these crystals will grow larger.



An atomic map of the protein crystal trypanthione created using X-ray diffraction.

These crystals can then be studied on the ground using a process called X-ray diffraction. Scientists can send a beam of X-rays through the crystal, and measure how the x-rays are bent by the atoms of the crystal. By studying the pattern made by the X-rays, they can then map the locations of the different atoms, allowing them to create a diagram of the protein's structure. With this as a guide, researchers can determine how the protein does its job.

Once this is known, researchers can then find ways to help or hinder a given protein by designing pharmaceutical compounds that will fit with its chemical "arms", instead of the hit and miss methods used in the past. Because a drug is targeted to a specific protein, less of the drug may be necessary as there is no "loss" to general reactions. The drug can be much more effective, because it reacts only with a specific protein. This also means that there are few, if any, side effects — which are caused when a drug reacts with other compounds in the body.



Earth-versus microgravity-grown crystals: Crystals of recominant human insulin grown in microgravity (right) are visibly larger than those grown at a ground-based laboratory (left, shown at the same magnification). The space-grown crystals also proved to be better ordered and optically clearer, making them more desirable for research. Dr. DeLucas was the principal investigator for this experiment, which flew on STS–60.

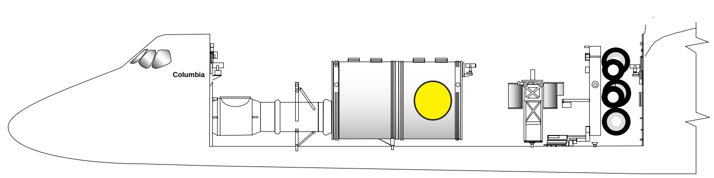
Previous Results

Because of the enormous potential this research offers, the Center for Biophysical Sciences and Engineering (formerly the Center for Macromolecular Crystallography or CMC), a NASA-sponsored Commercial Space Center located at the University of Alabama at Birmingham, has more than 60 major industry and academic partners using the low-gravity environment of space to grow protein crystals for use in drug design.

Protein-crystal growth experiments began flying on the Space Shuttle in 1985. Today, more than 40 protein-crystal growth payloads have flown, producing diffraction-quality crystals of many proteins. The CPCG-H first flew aboard the *International Space Station* during Expedition Two, launching aboard STS–100 in April 2001 and returning aboard STS–105 in August 2001. The data derived from each crystal analyzed is leading researchers closer understanding the structure and function of proteins.

Applications

Structural studies of microgravity-grown crystals have provided information for the development of new drugs. For example, studies conducted by Dr. DeLucas on crystals grown on Shuttle flights have been used in the design of inhibitors, which may serve as broad-spectrum antibiotics.



Approximate location of this payload aboard STS–107.

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